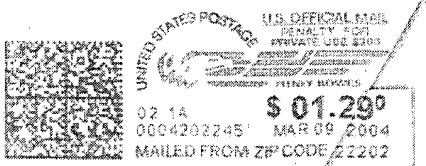
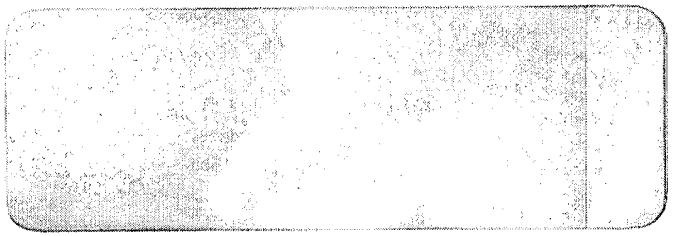
Organization 1600 Bldg./Room Remsen

U. S. DEPARTMENT OF COMMERCE
COMMISSIONER FOR PATENTS
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450
IF UNDELIVERABLE RETURN IN TEN DAYS

OFFICIAL BUSINESS



AN EQUAL OPPORTUNITY EMPLOYER



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,761	05/14/2001	Moon Hae Sunwoo	X-9338	6883

7590 03/09/2004

John S. Hale
GIPPLE & HALE
6665-A Old Dominion Drive
McLean, VA 22101

EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20042302

Application Number:09/853,761
Filing Date: May 14, 2001
Appelant(s): SUNWOO ET AL.

John S. Hale
Registration No. 25,209
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed November 14, 2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant(s) statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant(s) statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant(s) brief includes a statement that Claims 1-5 and 7-33 (Group I) and Claims 34-37 (Group II) do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

5,899,939	BOYCE et al.	05-1999
6,294,187	BOYCE et al.	09-2001

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-3, 5-9, 11-14, 27-31, 34, 36 and 37 stand finally rejected under 35 U.S.C. §103(a) over Boyce *et al.* (US '939) and Claims 4, 10, 15-26, 32, 33 and 35 stand finally rejected under 35 U.S.C. §103(a) over Boyce *et al.* (US '939) in view of Boyce *et al.* (US '187). This rejection is set forth in prior Office Action, Paper No. 6.

Boyce *et al.* teach a flexible bone sheet for use in the repair, replacement and/or augmentation of various portions of animal or human skeletal systems comprising a *unitary structure* of two or more layers: a demineralized cortical layer and another layer

of a different material, wherein the thickness of the layers range from about 0.5 mm to 20 mm (see reference column 1, lines 1-17); (column 3, lines 11-40).

Boyce *et al.* do not explicitly teach the specified residual calcium weight percentages. However, in view of the teachings of partially or fully demineralized bone, one could view the residual calcium weight percentage to be negligible (see '939 col. 1, lines 11-17) and ('187 col. 6, lines 15-29). Therefore, the determination of the content of residual calcium, is within the level of one skilled of the art.

Although Boyce *et al.* teach a bone sheet, they do not explicitly teach that the bone sheet be sterile. It is deemed obvious to one of ordinary skill in the pharmaceutical art to apply only sterile materials when used for implantation into human or animal skeletal systems.

Claims 4, 10, 15-26, 32, 33 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boyce *et al.* ('939) in view of Boyce *et al.* (US Pat. No. 6, 294,187), hereinafter ('187).

Boyce *et al.* ('939), as discussed above, teach a flexible bone sheet for use in the repair, replacement and/or augmentation of various portions of animal or human skeletal systems comprising a unitary structure of two or more layers: a demineralized cortical layer and another layer of a different material, wherein the thickness of the layers range from about 0.5 mm to 20 mm (see reference column 1, lines 1-17); (column 3, lines 11-40).

Boyce *et al.* do not teach hyaluronic acid in the bone composition. However, Boyce *et al.* ('187) teach an osteoimplant bone composition for use in the repair, replacement and/or augmentation of various portions of animal or human skeletal systems comprising demineralized cortical and cancellous portions, wherein mucopolysaccharides can also be added to the bone composition (see reference column 9, lines 6-15).

Therefore, it would have been obvious to one of ordinary skill in the art to add a mucopolysaccharide, such as hyaluronic acid, in a bone composition based on the suggestion of Boyce *et al.* '187. with the expected result of obtaining a bone particle composition that aids in bone formation.

Boyce *et al.* ('187) do not teach the instantly claimed molecular weights of hyaluronic acid (mucopolysaccharides). It is deemed obvious to one of ordinary skill in the art that suitable molecular weights could be obtained through routine or manipulative experimentation.

(11) Response to Argument

Appellant(s) urges that a prima facie case of obviousness has not been established against the claimed invention, based on the teachings of Boyce *et al.* ('939) for claims 1-3, 5, 7-9, 11-14, 27-31, 34, 36 and 37 and the teachings of Boyce *et al.* ('939) combined with Boyce *et al.* ('187) for claims 4, 10, 15-26, 32, 33 and 35.

Firstly, Appellant(s) urges "The Boyce *et al.* '939 reference is a bone derived implant of a load bearing composite structure which is made up of at least two

superimposed layers of fully mineralized or demineralized or partially demineralized cortical bone material adhesively secured or fastened to each other to form a single rigid structure which is then cut into shaped implants. At least one layer is a compression strength-imparting layer derived from non-demineralized cortical bone or cortical bone, which has been partially demineralized. The implant structure is constructed after demineralization of some layers has been undertaken with no degree of demineralization having been disclosed."

These arguments are not found to be persuasive. As delineated above, Boyce *et al.* ('939) teach a flexible bone sheet for use in the repair, replacement and/or augmentation of various portions of animal or human skeletal systems comprising a unitary structure of two or more layers: a demineralized cortical layer and another layer of a different material, wherein the thickness of the layers range from about 0.5 mm to 20 mm (see col. 1, lines 1-17 and col. 3, lines 11-40). Appellant(s) argues the degree of demineralization content of the Boyce *et al.* bone sheet. This argument was not found to be persuasive since the Examiner notes; the instant claims do not state that the bone sheet is fully demineralized. Instant independent claim one simply recites, "*demineralized bone*" as seen from Claim 1, line 3. The Boyce *et al.* patent teaches fully mineralized or partially demineralized cortical bone (col. 1, ln. 11-17). However, the instant claims do not recite the specific degree of demineralization. Therefore, Appellants' arguments were not found to be persuasive.

The Appellant(s) further urges, "The Boyce *et al.* ('939) implant is not made from a single piece of formed bone but from a composite of slices taken from a specific bone

or bones from the same donor. While the Examiner has characterized Boyce *et al.* '939 as comprising a unified structure of two or more layers which includes a demineralized cortical layer and another layer of a different material, this does not teach any of the layers to be cancellous or that the structure contains a cortical cancellous interface. Only cortical bone is used with the cancellous and cortical cancellous being wasted or subjected to granulation. These layers are optionally demineralized."

These arguments are not found to be persuasive. The instant claims recite a sterile flexible bone sheet comprising a continuous integral unitary sheet of demineralized natural bone with a cortical layer and a cancellous layer. The prior art teaches a unified structure of two or more layers, which includes the presence of a demineralized cortical layer and the presence of another layer of a different material. This other layer can be a cancellous layer. The argument that 'while a cortical layer is taught, a cancellous layer nor a structure containing a cortical cancellous interface is not taught' is not deemed persuasive by the Examiner since the instant claims do not rule out the fact that the cortical layer should *not* have pores. The Examiner notes, Boyce *et al.* (939), at column 2, lines 9-15, explicitly teaches that 'an object of the invention is to provide a bone implant possessing *a network of pores, apertures, perforations, channels or spaces which permits and encourages penetration* by endogenous and exogenous bone healing materials and blood supply, and simultaneously provides a means for incorporating one or more bone healing substances'. The term "cancellous", according to *Merriam Webster's Collegiate Dictionary* – Tenth Edition (Copyright 1999), is defined as 'intersecting osseous plates and bars in cancellous bone: *having a 'porous*

structure'. Accordingly, Boyce *et al.'s* teaching of 'a bone implant possessing a network of pores, apertures, perforations, channels or spaces' meets the Appellant's instant claim recitation of a "cancellous" layer.

The Appellant(s) next urges, "The Boyce *et al.* '939 composite structure can be anywhere from 2 to 200 layers overall preferably adhesively secured together, with a layer thickness ranging from about 0.5 to about 20 mm. The separate control layers of Boyce *et al.* '939 are held together through the use of biological compatible adhesives and mechanical fasteners such as pins, screws, dowels quite unlike the present invention which requires no adhesive or fasteners and makes maximum use of human bone. Thus, the present invention does not have the problem of layer shearing or separation or the problem of securing the mechanical fasteners in the layered product which are subjected to the various stresses which occur on the implant when the same is used in a human. In short, all that this reference teaches is the assembly of layers of cut cortical bone which are adhesively held together to provide a layered assembly which is then cut into the desired shape."

These arguments are not found to be persuasive. Although Boyce *et al.* '939 teaches that the bone-derived implant can possess from 2 to about 200 layers (see claim 21 of '939), the Examiner points out that instant claims utilize "comprising" claim language and thus, permits the inclusion of additional layers. Moreover, the differences argued by the Appellants are not reflected in the instant claim language, since the instant claims in and of themselves recite the use of layers (i.e., cortical layer, cancellous layer). Even further, the prior art teach a bone-derived implant that is

entirely unitary in structure, as similarly desired by the Appellant(s). With respect to the argument that 'unlike Boyce *et al.* '939, the present invention requires no adhesives or fasteners', the Examiner has not been persuaded by this argument since the prior art clearly teach a bone-derived implant that exhibits good load-bearing properties (see, for instance, Abstract).

The Appellant(s) urge, "Furthermore, Boyce *et al.* '939 do not teach residual calcium left after demineralization because the bone is fully mineralized to achieve osteoinductiveness."

These arguments are not found to be persuasive. The Examiner points out that instant claims recite, 'unitary sheet of *demineralized* natural bone' and do not recite '*fully* demineralized bone'. Hence, the amount of residual calcium left after demineralization was not deemed pertinent to the formulation.

Next, the Appellant(s) traversed the Examiner's rejection of Claims 4, 10, 16-26, 32, 33 and 35 as being obvious and unpatentable over the combined teachings of Boyce *et al.* ('939) in view of Boyce et al. ('187).

The Appellant(s) urge, "As previously noted the Boyce *et al.* '939 reference is a bone derived implant of a load bearing composite structure which is made up of at least two superimposed layers of fully mineralized or demineralized or partially demineralized cortical bone material adhesively secured or fastened to each other to form a single rigid structure which is then cut into shaped implants. The implant structure is constructed after demineralization has been undertaken with no degree of

demineralization having been disclosed. The Boyce *et al.* '939 implant is not made from a single piece of formed bone but from a composite of slices taken from the control layer. Only cortical bone is used with the cancellous and cortical cancellous being wasted or subjected to granulation. These layers are optionally demineralized. The Boyce *et al.* '939 composite structure can be anywhere from 2 to 200 layers overall and are adhesively secured together, with a thickness ranging from about 0.5 to about 20 mm and a noted compressive strength. The separate control layers are held together through the use of biological compatible adhesives and mechanical fasteners such as pins, screws, dowels, quite unlike the present invention which requires no adhesive or fasteners and makes maximum use of human bone. Example 1 of Boyce *et al.* '939 is directed toward slices of mineralized bone and Example 2 is directed toward half of the slices being fully demineralized. As noted in Examples 1 and 2, the slices are held together with cyanoacrylate adhesive. Example 3 is directed to longitudinally cut fully mineralized bars arranged in a lattice structure. In short, all that this reference teaches is the assembly of layers of cut cortical bone, which are adhesively held together to provide a layered assembly which is then cut into the desired shape. The Boyce *et al.* '939 reference teaches away from the present invention. Furthermore, Boyce *et al.* '939 does not teach residual calcium left after demineralization because the bone is fully demineralized to achieve osteoinductiveness. The Examiners' response that routine or manipulative experimentation could obtain the ranges of residual calcium is without merit. Published technical studies have shown that residual calcium has a benefit in the bone healing process."

These arguments are not found to be persuasive. As delineated above, the Boyce *et al.* '939 reference teaches a flexible bone sheet for use in the repair, replacement and/or augmentation of various portions of animal or human skeletal systems comprising a unitary structure of two or more layers: a demineralized cortical layer and another layer of a different material, wherein the thickness of the layers range from about 0.5 mm to 20 mm. Appellant(s) argues the degree of demineralization content of the Boyce *et al.* '939 bone sheet. This argument was not found to be persuasive since the Examiner notes; the instant claims do not state that the bone sheet is *fully* demineralized. The instant claims simply recite, 'unitary sheet of *demineralized* natural bone' and do not recite '*fully* demineralized bone' or do not include a specific amount of demineralization. Hence, the amount of residual calcium left after demineralization was not deemed particularly pertinent to the formulation. Appellant then urges the number of layers contained in the Boyce *et al.* '939 implant (2-200 layers) and that the layers are held together through the use of biological compatible adhesives and mechanical fasteners whereas the present invention which requires no adhesive or fasteners and makes maximum use of human bone. The Examiner was not persuaded by this argument since the instant claims utilize "comprising" claim language and thus do not exclude the use of additional layers. Moreover, the differences argued by the Appellant(s) are not reflected in the instant claim language, since the instant claims in and of themselves recite the use of layers (i.e., cortical layer, cancellous layer). Further, the prior art teach a bone-derived implant that has good

load-bearing properties. Hence, the Appellants' arguments were not found to be persuasive.

Next, the Appellant(s) urge, "The Boyce *et al.* '187 patent simply teaches a rigid osteoimplant bone composition formed of shaped compressed bone particles having a bulk density of greater than about 0.7/g/cm^3. These powdered bone particles range in average particle size from about 0.05 to about 1.2 cm in size and are obtained by milling or shaving the surface of an entire bone with at least 60% of the bone particles being elongated. Preferably at least 60% and most preferably at least about 90% by weight of the bone particles are elongate. The particles possess an average median length to median thickness ratio of from about 1:1 to about 3:1. Particles are formed by milling whole bone to produce fibers, chipping whole bone, cutting whole bone, fracturing whole bone in liquid nitrogen or otherwise disintegrating the bone tissue. The bone particles employed in the composition can also be obtained from cortical, cancellous and/or corticocancellous bone. Preferably, the bone particles are obtained from cortical bone of allogenic origin. Compressive forces of about 2,500 to 60,000 psi preferably ranging from 4 to about 72 hours in addition to heating are applied to the bone particles in a mold to produce a "hard chalk-like material" (Col. 11, line. 66). The osteoimplant can then be lyophilized and crosslinked. There is no teaching using the natural layer of cancellous bone or cortical cancellous interface as part of a bone sheet in a continuous integral sheet of bone used for surgical repair. Indeed, the prevailing view was that only cortical bone could be used for strength reasons. However, it has been found that cancellous bone can be used and that it has excellent osteoinductive properties. The

'187 reference does not teach or suggest the present invention which has a continuous sheet of demineralized bone with a cortical and cancellous layer taken from a single bone. Applicants thus submit that the cited references in combination do not teach or obviate the present invention. There is no teaching of the cancellous and cortical layers and no teaching of the cancellous cortical interface section, indeed there is only an inferential mention that particles having such composition can be used. One cannot combine references, one of which uses a sandwich construction of layers of cut cortical bone held together with adhesives or fasteners with an implant formed of elongate ground particles held together by the use of high compressive forces and heat to arrive at the present invention except through hindsight and conjecture. Obviousness must be based on what is shown in the prior art. There is also no teaching of the method claimed nor could one possibly combine the two references, slicing of cortical bone and adhesively fixing the layers together of Boyce *et al.* '939 and the slurry and compression of particles of Boyce *et al.* '187 to arrive at the claimed method."

These arguments are not found to be persuasive. The Appellant(s)' argument that 'There is no teaching using the natural layer of cancellous bone or cortical cancellous interface as part of a bone sheet in a continuous integral sheet of bone used for surgical repair' and that 'The cited references in combination do not teach or obviate the present invention' is disagreed upon since the primary reference (Boyce *et al.* '939) teach a flexible bone sheet for use in the repair, replacement and/or augmentation of various portions of animal or human skeletal systems comprising a unitary structure of two or more layers: a demineralized cortical layer and another layer of a different

material, wherein the thickness of the layers range from about 0.5 mm to 20 mm. Boyce *et al.* '939 are lacking in the sense that they do not teach hyaluronic acid in the bone composition. Boyce *et al.* ('187) resolves this only deficiency of Boyce *et al.* '939 and was relied upon for the teaching of an osteoimplant bone composition for use in the repair, replacement and/or augmentation of various portions of animal or human skeletal systems comprising demineralized cortical and cancellous portions, wherein mucopolysaccharides can also be added to the bone composition (column 9, lines 6-15). The bone particles employed in Boyce *et al.* '187 can also be obtained from cortical, cancellous and/or corticocancellous bone.

In response to Appellant(s) argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The Appellants' argument that 'The references cannot be combined, since one uses a sandwich construction of layers of cut cortical bone held together with adhesives or fasteners whereas the other is an implant formed of elongate ground particles held together by the use of high compressive forces and heat' was also not persuasive since the primary reference, Boyce *et al.* '939 while teaching a bone-derived load-bearing implant comprising a plurality of superimposed layers (cortical layer and another layer of

a different material), that are assembled into a unitary structure, also teaches at least one layer in the structure being a compression-strength imparting layer fabricated from non-demineralized cortical bone or partially demineralized cortical bone (see col. 2, lines 23-29 & col. 3, lines 35-40). The secondary reference, Boyce *et al.* '187, also teaches the use of high compressive forces for obtaining a load-bearing osteoimplant comprising a shaped, compressed composition of bone particles, rather than a bone sheet. Furthermore, the secondary reference (Boyce *et al.* '187) was relied upon for the teaching that it is obvious to include mucopolysaccharides, such as hyaluronic acid in bone compositions, as taught by Boyce et al. '187, with the expected result of obtaining a bone particle composition that aids in bone formation. Hence, the combination of the two Boyce *et al.* references clearly obviates the present invention.

Next, the Appellant(s) traversed the Examiner's rejection of Claims 1 and 4 under the judicially created doctrine of Double Patenting over Claims 1 and 10 of U.S. Pat. No. 6,326,018 B1 stating, "The '018 patent is directed toward a totally different invention. A double patenting rejection of the obvious type is analogous to the non-obviousness requirement of 35 U.S.C. 103 in that no person of ordinary skill in the art would conclude that the invention defined in the claims in issue is an obvious variation of the claimed invention defined in the claims of the '018 patent. However, only the claims are compared and not the whole document as would be required in a normal 35 U.S.C. 103 rejection."

These arguments are found to be persuasive. Accordingly, the Double Patenting rejection over Claims 1 and 4 are being withdrawn.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Humera N. Sheikh - Group 1615

Humera N. Sheikh

hns
March 4, 2004

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Conferees
Thurman K. Page (SPE)
Kishore S. Gollamudi, Ph.D.
Humera N. Sheikh

G S Kishore

Gollamudi S. Kishore, PhD
Primary Examiner
Group 1600

JOHN S. HALE
GIPPLE & HALE
6665-A OLD DOMINION DRIVE
MCLEAN, VA 22101